

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

DMB

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[Docket No. 00N-1494]

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Agency Information Collection Activities; Submission for OMB Review; Comment Request; Medical Devices; Classification/Reclassification; Restricted Devices: Analyte Specific Reagents

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing that the proposed collection of information listed below has been submitted to the Office of Management and Budget (OMB) for review and clearance under the Paperwork Reduction Act of 1995.

DATES: Submit written comments on the collection of information by *[insert date 30 days after date of publication in the Federal Register]*.

ADDRESSES: Submit written comments on the collection of information to the Office of Information and Regulatory Affairs, OMB, New Executive Office Bldg., 725 17th St. NW., rm. 10235, Washington, DC 20503, Attn: Wendy Taylor, Desk Officer for FDA.

FOR FURTHER INFORMATION CONTACT: Peggy Schlosburg, Office of Information Resources Management (HFA-250), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-1223.

SUPPLEMENTARY INFORMATION: In compliance with 44 U.S.C. 3507, FDA has submitted the following proposed collection of information to OMB for review and clearance.

**Medical Devices: Classification/Reclassification; Restricted Devices; Specific Reagents—21
CFR Part 809 (OMB Control No. 0910–0361)—Extension**

Section 502 of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 352) establishes certain labeling requirements for devices including requirements that the labeling not be false or misleading in any particular, that the labeling contain the established name for the device, and that the labeling contain adequate directions for use. Section 520(e) of the act (21 U.S.C. 360j(e)) provides that FDA may restrict the sale, distribution, or use of a device, if FDA determines that there cannot otherwise be reasonable assurance of its safety and effectiveness. Section 502(q) and (r) of the act authorizes FDA to regulate the advertising of devices that are restricted under section 520(e) of the act.

FDA restricts distribution of analyte specific reagents (ASR's) to laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) as qualified to perform high complexity testing, to manufacturers of in vitro diagnostic products, and to organizations that use the tests for reasons other than providing diagnostic information to practitioners and patients. FDA has established certain labeling requirements for suppliers of ASR's and certain requirements regarding advertising and promotional materials for ASR's. FDA believes the labeling requirements and restrictions on advertising and promotion are necessary to ensure that laboratories developing tests from ASR's have sufficient information to use the ASR's appropriately and to limit specific claims by manufacturers, because these ASR's are intended to be used as ingredients in a variety of ways by laboratories qualified to do high complexity testing.

The most likely respondents to this information collection will primarily be medical device manufacturers of in vitro products, clinical laboratories, and other manufacturers of ASR's.

In the **Federal Register** of September 14, 2000 (65 FR 55633), the agency requested comments on the proposed collection of information. One comment, discussing three separate issues, was received.

1. The comment first asked that medical device manufacturers provide basic laboratory instructions for use and warn against uses that are not appropriate for the particular ASR.

FDA was not persuaded by this comment. The intention of the ASR rule is to ensure that laboratories using these products to develop in-house or “home brew” tests take full responsibility for the development of the “home brew” test and for the characterization of test performance for the ASR based test. ASR use is restricted to high-complexity laboratories under the CLIA which have the ability to develop tests based on their own experience or the medical literature. The instructions for use in different laboratories using ASR’s would be expected to vary with the experience of the laboratory and with the information obtained during test development and characterization.

If a medical device manufacturer wishes to provide laboratory instructions on product use, this is acceptable. However, this is evidence that a kit or system is being marketed rather than used as an ASR or building block for an assay. Such a device would not be exempt from premarket review by FDA.

2. The comment further indicated that a guidance or written clarification as to the scope of appropriate warnings and precautions would be helpful.

FDA does not believe such guidance or written clarification is necessary. The regulation in 21 CFR 809.10(e)(1)(v) requires “A statement of warnings or precautions for users as established in the regulations contained in 16 CFR part 1500 and any other warnings appropriate to the hazard presented by the product.” Hazards in use of laboratory reagents are well known and the subject of multiple book chapters and a voluntary standard. The information required which includes, as appropriate, warnings regarding flammability, toxicity, teratogenicity, and carcinogenicity are well known by both manufacturers and laboratory users. Additional information on these would duplicate existing commonly used information sources and conditions of art.

3. Finally, the comment indicated that product support dictates that information be provided to users on proper set up of instruments, preparation of samples, and the generation of good quality data.

FDA agrees that the information cited is of key importance in test performance. For “home brew” tests, however, the responsibility for developing this information is clearly assigned to the laboratory, not to the manufacturer of the ASR. The only responsibility the ASR manufacturer has is to produce product according to the quality system regulations, to label it clearly as a building block for use in “home brew” assays, and to restrict sales to high complexity laboratories. These laboratories by law have the personnel standards, proficiency testing, quality control and quality assurance requirements, and requirements for controlled operating environments needed in the development of quality “home brew” tests.

FDA estimates the burden of this collection of information as follows:

TABLE 1.—ESTIMATED ANNUAL REPORTING BURDEN¹

21 CFR Section	No. of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Hours
809.10(e)	300	25	7,500	1	7,500
809.30(d)	300	25	7,500	1	7,500
Total					15,000

¹ There are no capital costs or operating and maintenance costs associated with this collection of information.

The number of affected establishments was derived by asking five organizations for estimates and averaging their responses to arrive at an average number of establishments affected by this rule. These organizations included the largest trade association representing the in vitro diagnostic industry, the larger trade association for nonbiotechnology products, two of the largest organizations representing laboratory professionals, and the in vitro diagnostic company instrumental in providing industry input into the implementation of this rule. Three of the five organizations had access to data bases allowing them to project estimates of establishments likely to manufacture or supply ASR's. These estimates ranged from 100 to 500. FDA therefore used the average of 300 ASR manufacturers and suppliers subject to the reporting requirements from these estimates.

FDA relied upon the five trade organizations in estimating the number of ASR's manufactured. Again, three of the organizations offered information from their data bases. Estimates for the

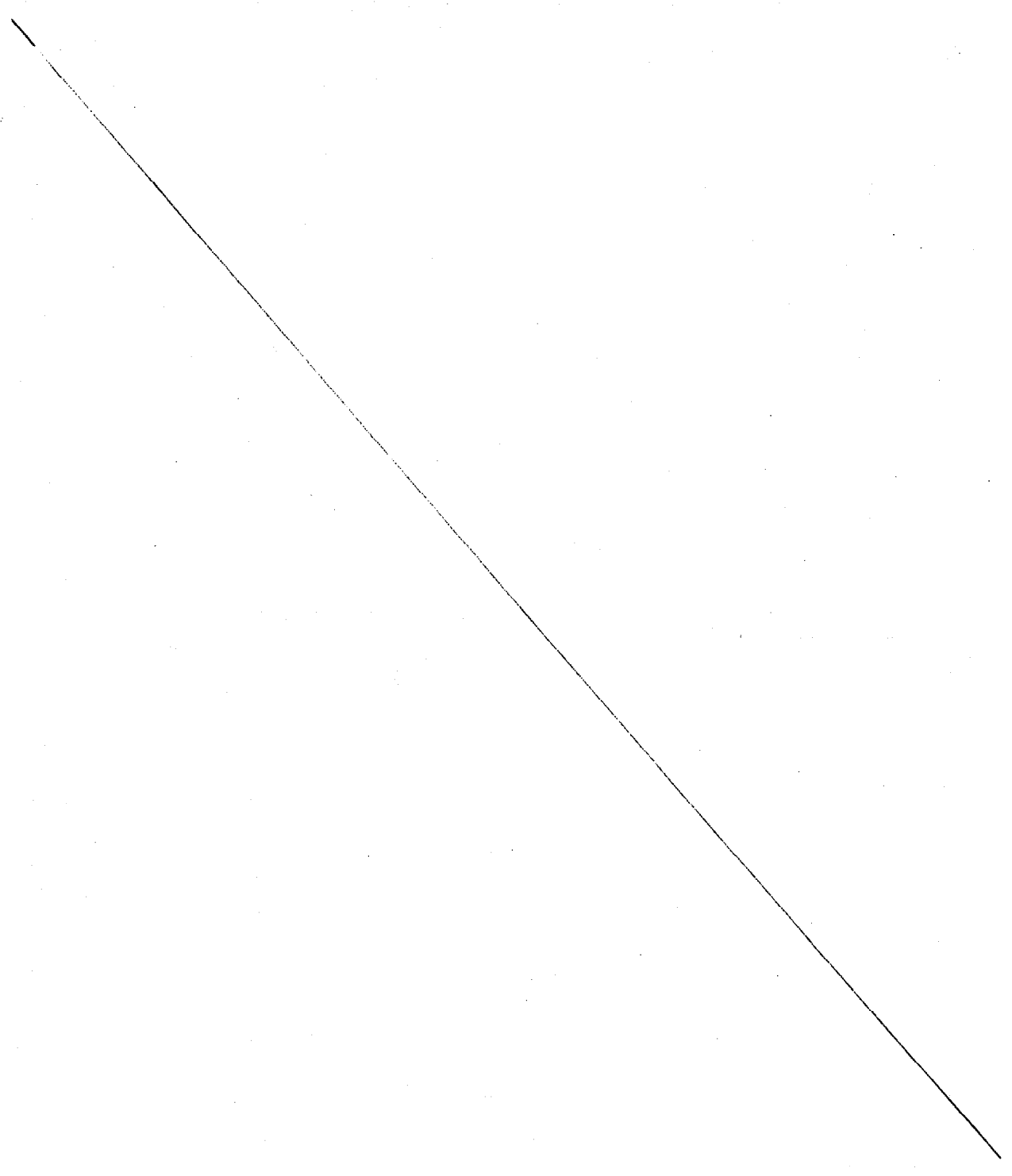
number of ASR's ranged from 5,000 to 10,000, with the average being 7,500. FDA therefore estimates that approximately 7,500 ASR's are currently being manufactured.

In order to ascertain the number of ASR's manufactured by each respondent, FDA used the average number of ASR's manufactured and divided it by the number of ASR manufacturers ($7,500 \div 300$). Consequently, the estimate of the number of ASR's manufactured by each respondent is approximately 25. (In the previously published final rule of November 21, 1997 (62 FR 62243), the total number of ASR's were listed as "1," and the number of respondent burden hours associated with ASR's were "25." These numbers were reversed in error.)

FDA estimates that for each ASR, it would take approximately 1 hour to design a new label to conform with the new requirements and approximately 3 hours to provide management review and legal and marketing sign-off. Therefore, FDA estimates that the total number of hours needed to design/review labels is approximately 100 hours per respondent (25×4). The total number of hours to design/review labels by all establishments is estimated at 30,000 (100×300). However, these estimates do not take into account economies of scale in designing and revising the labeling on ASR's, which should reduce the time expended in ASR labeling by 75 percent. Consequently, FDA estimates that the total number of reporting hour burden for designing/review of labeling is approximately 25 hours per respondent instead of 100. FDA also estimates that the total reporting hour burden is approximately 7,500 hours instead of 30,000.

FDA estimates for each ASR, it would take approximately 1 hour to rewrite the professional materials to ascertain compliance with the new requirements and approximately 4 hours to obtain management review of rewritten materials and legal and marketing sign-off. FDA therefore estimates that the total number of hours to rewrite/review promotional materials is approximately 125 hours per respondent (25 ASR's per respondent \times 5 hours for review). The total reporting hours for all ASR's is estimated at 37,500 (125 hours \times 300 manufacturer/suppliers). However, this estimate does not take into account economies of scale. Often the promotional materials are a catalogue of products. FDA estimates that entities spend approximately 20 percent of the time

devoted to reporting ASR's (37,500 hours) ascertaining that the promotional materials meet the new requirements. Consequently, FDA estimates that the total number of reporting hour burden for rewriting/reviewing promotional materials under 21 CFR 809.30(d) is approximately 25



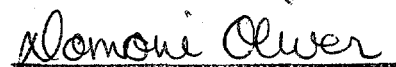
hours per respondent (125 x .20), and estimates that the total reporting hour burden for promotional materials is approximately 7,500 hours (37,500 x .20).

Dated: December 28, 2000



Margaret M. Dotzel,
Associate Commissioner for Policy.

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